DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

JUL 28 2010

I-011740-P-0010-HF (AA)

U.S. Fish & Wildlife Service
Aqquatic Animal Drug Approval partnership Program
Attention: Dr. David Erdahl
Branch Chief, AADAP Program
4050 Bridger Canyon Road
Bozeman, MT 59715

Subject: INAD 011740-P-0010 – Benzocaine for finfish. Genetic Toxicology Studies – Human Food Safety *Technical Section incomplete.*

Dear: Dr. Erdahl

We are providing you with a Human Food Safety Technical Section Incomplete letter in response to your submissions I-011740-P-0010-HF dated January 28, 2010. We reviewed the genetic toxicology reports on benzocaine included in this submission. Our conclusions are provided below:

A. Bacterial Reverse Mutation Assay. Test Article: Benzocaine: Author: V. O. Wagner and M. R. VanDyke. BioRelinace, Rockville, MD. Study No: AC30AY.503.BTL. December 31, 2009.

CVM concurs with your conclusion that under the conditions of this study, benzocaine did not cause a positive response in the presence and absence of Aroclor-induced rat liver S9.

B. In Vitro Mammalian Cell Gene Mutation Test (L5178Y/TK$^{+/-}$ Mouse Lymphoma Assay): Author: Jane J. Clarke, BioReliance, Rockville, Maryland. BioReliance Study Number: AC30AY.704BTL. January 4, 2010.

CVM concurs with your conclusion that under the conditions of this study, benzocaine is negative in the L5178Y/TK+/- Mouse Lymphoma Mutagenesis Assay.

C. Mouse Bone Marrow Erythrocyte Micronucleus Test Following Oral Administration of Bezocaine. Authors: Krsmanovic, L. and Divi, K. BioReliance, Rockville, Maryland. BioReliance Study Number: AC30AY.123MBTL. January 26, 2010.

CVM concurs with your conclusion that "Under the conditions of the assay described in this report, a single oral administration of benzocaine at doses up to 2000 mg/kg did not induce a

significant increase in the incidence of micronucleated polychromatic erythrocytes in bone marrow and was concluded to be negative in the micronucleus test using male ICR mice."

D. Validation of an Analytical Method for the Determination of Benzocaine: Authors: P. Atkins and J. Followeiler. BioRelinace, Rockville, MD. Study No: AC30AY.GTCHEM.BTL. December 31, 2009.

This report contains the validation of the analytical method that is used to determine the concentration of benzocaine in the dosing solutions used during the genotoxicity tests. The dosing solutions were prepared in either dimethylsulfoxide (DMSO) or corn oil.

We consider your validation of an analytical method is adequate for the determination of benzocaine concentrations in the dosing solutions prepared in dimethylsulfoxide or corn oil.

If you submit correspondence relating to this letter, your correspondence should reference the date and the principal submission identifier found at the top of this letter. If you have any questions or comments, please contact me at phone number 240-276-8225. You may also contact Dr. Kevin Gaido, Acting Toxicology Team Leader, HFV-153 at 240-276-8212.

Sincerely,

Karen B. Ekelman, Ph.D.
Director, Division of Human Food Safety
Office of New Animal Drug Evaluation
Center for Veterinary Medicine